

In the claims:

Please amend claims as follows:

1-20. (Cancelled)

21. (Currently amended) A non-human transgenic organism having a transgene integrated into the genome of the organism and also having a *tet* operator-linked gene in the genome of the organism, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the organism operatively linked to a polynucleotide sequence encoding a fusion protein which activates transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which is a mutated Tet repressor that binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline analogue operatively linked to a second polypeptide which activates transcription in eukaryotic cells,

said *tet* operator-linked gene confers a detectable and functional phenotype on the organism when expressed in cells of the animal organism,

said transgene is expressed in cells of the animal organism at a level sufficient to produce amounts of said fusion protein that are sufficient to activate transcription of the *tet* operator-linked gene; and

in the presence of tetracycline or a tetracycline analogue in the organism, said fusion protein binds to the *tet* operator-linked gene and activates transcription of the *tet* operator linked gene such that the *tet* operator-linked gene is expressed at a level sufficient to confer the detectable and functional phenotype on the animal organism, wherein the level of expression of the *tet* operator-linked gene can be downmodulated by depleting tetracycline or a tetracycline analogue from the animal organism.

22. (Currently amended) A non-human transgenic organism having a transgene integrated into the genome of the organism and also having a *tet* operator-linked gene in the genome of the organism, wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the organism operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene,

the fusion protein comprises a first polypeptide which is a mutated Tet repressor that binds to a *tet* operator sequence in the presence of tetracycline or a tetracycline

analogue operatively linked to a second polypeptide which inhibits transcription in eukaryotic cells,

said *tet* operator-linked gene confers a detectable and functional phenotype on the organism when expressed in cells of the organism,

said transgene is expressed in cells of the organism at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

in the presence of tetracycline or a tetracycline analogue in the organism, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the *tet* operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by depleting tetracycline or a tetracycline analogue from the organism.

23. **(Currently amended)** A non-human transgenic organism having a transgene integrated into the genome of the organism. and also having a *tet* operator-linked gene in the genome of the organism., wherein:

the transgene comprises a transcriptional regulatory element functional in cells of the organism. operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene,

said fusion protein comprises a first polypeptide that is a Tet repressor, operably linked to a heterologous second polypeptide which inhibits transcription of said *tet* operator-linked gene in eucaryotic cells,

said *tet* operator-linked gene confers a detectable and functional phenotype on the organism when expressed in cells of the organism.,

said transgene is expressed in cells of the organism. at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

in the absence of tetracycline or a tetracycline analogue in the organism., said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the *tet* operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by administering tetracycline or a tetracycline analogue to the organism..

24. **(Original)** The organism of claim 21, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

25. **(Original)** The organism of claim 24, wherein the mutated Tet repressor is a mutated Tn10- derived Tet repressor having an amino acid substitution at at least one

amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102.

26. **(Original)** The organism of claim 24, wherein the mutated Tn10-derived Tet repressor comprises an amino acid sequence shown in positions 1 to 207 of SEQ ID NO: 2.

27. **(Original)** The organism of claim 21, wherein the second polypeptide of the fusion protein comprises a transcription activation domain of herpes simplex virion protein 16.

28. **(Original)** The organism of claim 22, wherein the second polypeptide of the fusion protein comprises a transcriptional silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tup1 protein complex, the Drosophila protein even-skipped, SIR1, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4 and ZF5.

29. **(Original)** The organism of claim 21, wherein expression of the transgene is regulated by at least one *tet* operator sequence.

30. **(Original)** The organism of claim 21, wherein expression of the transgene is regulated by at least one virally-derived regulatory element.

31. **(Original)** The organism of claim 21, wherein expression of the transgene is regulated by at least one tissue-specific regulatory element.

32. **(Original)** The organism of claim 21, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

33. **(Original)** The organism of claim 32, wherein the at least one *tet* operator sequence is operatively linked upstream of the second transgene.

34. **(Original)** The organism of claim 32, wherein the at least one *tet* operator sequence is operatively linked downstream of the second transgene.
35. **(Original)** The organism of claim 21, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.
36. **(Currently amended)** The organism of claim 21, which is selected from the group consisting of: a mouse, a cow, a sheep, or a pig, ~~or a plant~~.